

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-4 and 6-14 are pending in the application, with claim 1 being the independent claim. Claim 5 was previously cancelled. Claims 11-14 were previously withdrawn. Claim 1 has been amended. Support for the amendment to claim 1 can be found throughout the application as filed, e.g., in originally filed claims 1 and 5. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Rejections under 35 U.S.C. § 103 in view of Hoffman***

Claims 1, 2, 4, 6, 7, 9 and 10 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Pat. No. 7,737,108 ("Hoffman"). Applicants respectfully traverse this rejection.

The Examiner asserts that "[a]s a first matter, the instant claims do not exclude a hydrophobic component. Therefore, the inclusion of hydrophobic components in the compositions taught by Hoffman does not indicate that the compositions are distinct from those instantly claimed." *See* Office Action at page 4. Applicants respectfully disagree.

Solely in an effort to advance prosecution of the current application, claim 1 has been amended to recite "[a] conjugate for gene transfer, consisting essentially of an oligonucleotide intended to be transferred into a target cell and a hydrophilic polymer, wherein an end of the oligonucleotide is covalently linked to the hydrophilic polymer via an acetal bond." See claim 1, *supra*, emphasis added. Therefore, amended claim 1 does not include a hydrophobic component as an essential component.

The Examiner further asserts that Hoffman clearly teaches that the hydrophilic component, *i.e.* PEG, can be covalently linked to an oligonucleotide drug via an acetal bond. See Office Action at page 4. As Applicants previously showed, Hoffman requires that if a hydrophilic polymer (e.g., PEG) is present, it must be conjugated to a hydrophobic polymer. See, e.g., Hoffman at col. 4, ll. 1-2.

This is exemplified in Fig. 3, Example 2, and claim 1 of Hoffman. Specifically, in Fig. 3, PEG (*i.e.*, the hydrophilic polymer) or drug is linked to the membrane-disruptive polymer backbone (*i.e.*, hydrophobic polymer) via an acid degradable linker. In Example 2, a terpolymer of DMAEMA, BMA, and styrene benzaldehyde was used as a membrane -disruptive backbone, and the hydrophilic polymer, PEG, was linked to the terpolymer. In claim 1, the claim recited that the composition has the constitution in which hydrophobic component was linked to the hydrophilic component.

Since the composition of Hoffman requires a hydrophobic component as an essential component, and amended claim 1 does not include a hydrophobic component as an essential component, not only is the composition distinct, but the mechanism of action between Hoffman and the claimed invention is different. Thus, one of skill in the art

would not have looked to Hoffman and predicted the result of the present invention. Therefore, the Examiner has not established a *prima facie* case of obviousness against amended claim 1.

At least for the above reasons, claim 1 is patentable over Hoffman. Claims 2, 4, 6, 7, 9 and 10 depend either directly or indirectly from claim 1, and are patentable over Hoffman for the same reasons.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 2, 4, 6, 7, 9 and 10 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hoffman.

***Rejections under 35 U.S.C. § 103 in view of Hoffman and Tullis***

Claims 1-4 and 6-10 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hoffman in view of U.S. Pat. No. 4,904,582 ("Tullis"). Applicants respectfully traverse this rejection.

As described above, Hoffman does not teach or provide any reason for a conjugate consisting essentially of an oligonucleotide and a hydrophilic polymer, wherein the end of the oligonucleotide is covalently linked to the hydrophilic polymer via an acetal bond.

Tullis does not cure the deficiencies of Hoffman. Namely, Tullis does not teach or provide any reason for a conjugate consisting essentially of an oligonucleotide and a hydrophilic polymer, wherein the end of the oligonucleotide is covalently linked to the

hydrophilic polymer via an acetal bond. Therefore, the Examiner has not established a *prima facie* case of obviousness against amended claim 1.

At least for the above reasons, claim 1 is patentable over Hoffman in view of Tullis. Claims 2-4 and 6-10 depend either directly or indirectly from claim 1, and are patentable over Hoffman in view of Tullis for the same reasons.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-4 and 6-10 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hoffman in view of Tullis.

***Nonstatutory Double Patenting Rejection***

Claims 1-4 and 6-10 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1, 3, 8, 10, and 13 of co-pending U.S. Application No. 11/651,011 in view of Hoffman. Applicants respectfully request that this nonstatutory obviousness-type double patenting rejection be held in abeyance until allowable subject matter in the present application or co-pending Application No. 11/651,011 is indicated.

***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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